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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,036	03/16/2004	Stephen D. Pacetti	50623.311	7967

7590 11/12/2009
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EXAMINER

HELM, CARALYNNE E

ART UNIT	PAPER NUMBER
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1615

MAIL DATE	DELIVERY MODE
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11/12/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/805,036	Applicant(s) PACETTI, STEPHEN D.	
	Examiner CARALYNNE HELM	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-41 is/are pending in the application.
- 4a) Of the above claim(s) 7-12, 16-18, 28-33 and 37-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 13-15, 19-27, 34-36, 40 and 41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

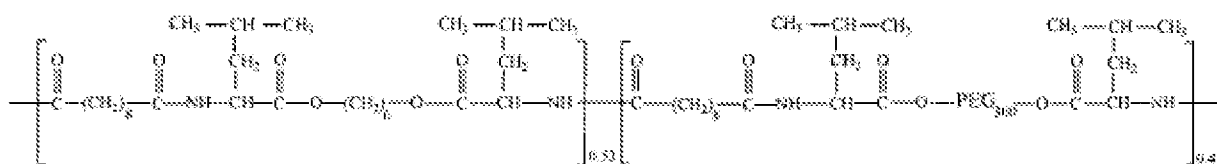
Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

To summarize the current election, applicant elected the species where the polymer is polymer 23 (depicted below) and the reagents used to produce it are compounds 1, 5, and 9.



The claims that were withdrawn from consideration are 7-12, 16-18, 28-33, and 37-39.

NEW REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of *Graham v. John Deere Co.* have been fully considered and analyzed in the rejections that follow.

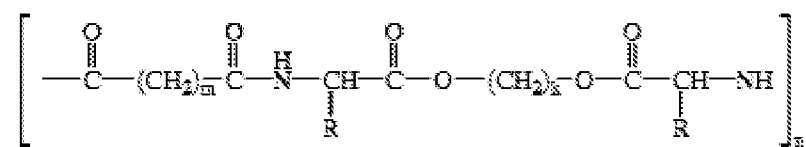
Claims 1, 3-6, 13-15, 19-21, 23-27, 34-36, and 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katsarava et al. (previously cited) in view of Katsarava et al. (previously cited – henceforth Katsarava et al. reference B), Nagata (previously cited) and Bezemer et al. (Journal of Biomedical Materials Research 2000 52:8-17).

Claims 1, 3-6, and 13-15 recite a product-by-process. “[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In *re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. Here the only structure conferred by the process steps of the claims is the chemical structure of the polymer in the coating. Thus the prior art need only teach or make obvious the polymer structure in the coating, regardless of the process used to produce, it in order to meet the limitations drawn to the polymeric material.

Katsarava et al. teach biodegradable poly(ester amide) polymers made from amino acids that are used to coat implantable medical devices and provide controlled release of biologically active substances (see paragraphs 15-16, 45, and 47). In

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particular, the compounds are made from the polymerization of a diol (D) with a dicarboxylic acid (C) and an alpha-amino acid (A) (see paragraph 16). The resulting polymers have monomers arranged to form DACA (formula II) or CADA (formula I). In particular, poly(ethylene glycol) as well as a C₆ alkylene diol are envisioned as diols (D) (see paragraphs 10-14, 17, and 19-21; instant claims 1, 3, 13, 19-21, 24, 34, and 40-41). Leucine is envisioned as a particularly preferred amino acid (A) (see paragraphs 10-14 and 25; instant claims 1, 3-6, 13-15, 19-21, 24-27, 34-36, and 40-41). A linear C₈ α, ω dicarboxylic acid is taught as a preferred dicarboxylic acid (C) (see paragraphs 10-14, 18-19, and 22; instant claims 1, 19-21, and 40-41). A particular set of polymers with CADA configured units that were known are depicted in formula I (see below)



[0011] where

[0012] k=2, 3, 4, or 6

[0013] m=4 or 8, and

[0014] R=CH(CH₃)₂, CH₂CH(CH₃)₂,
 CH(CH₃)CH₂CH₃, (CH₂)₃CH₃, CH₂C₆H₅, or
 (CH₂)₃SCH₃.

Katsarava et al. do not explicitly teach the elected polymer with two different CADA units such that one has poly(ethylene glycol) as the diol while the other utilizes a hexyl moiety as the diol.

Katsarava et al. reference B teaches poly(ester amide) polymers that are composed of CADA monomers and are the form of formula I (see Schemes 1-3). One

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particular polymer (termed 8-L-Leu-6) taught has $m = 8$, $k=6$ and $R = \text{iso-butyl}$ thereby teaching a monomer where C is a linear $C_8 \alpha, \omega$ dicarboxylic acid, A is leucine, and D is a C_6 alkylene (hexyl) diol (see Table II compound 10). This is one of the CADA monomers in the elected polymer. This polymer is produced by the polymerization of a monomer constructed by the condensation of an amino acid with a diol whose product is then reacted with a dicarboxylic acid (see Schemes 1 and 2; instant claims 21 and 24-27) Katsarava et al. reference B also teaches that degradation of their polymers is enzymatically catalyzed (see table VIII).

Nagata teaches that aliphatic polyesters were known degradable synthetic polymers whose degradation could be uneven due to their hydrophobicity and high melting point (see page 33 column 1 paragraph 1). Nagata also teach that the introduction of poly(ethylene glycol) (PEG) segments into the polymer backbone would solve this issue (see page 33 column 1 paragraph 1). Nagata demonstrates that the presence of a low molecular weight PEG (PEG 200) allows for degradation to occur via both a standard hydrolytic route and an enzymatically catalyzed route (see figure 4). In addition, the length of the PEG chain and the proportion of PEG in the polymer determine the polymers susceptibility to enzyme catalyzed degradation, thereby allowing one of ordinary skill to control or tune the polymer degradation to a desired end point (e.g. slower or faster) (see figure 4).

Bezemer et al. teach that the application of biodegradable amphiphilic block copolymers as drug delivery systems was known (see page 8 column 1 paragraph 1). They go on to teach the use of PEG as a hydrophilic segment in such polymers and

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hydrophobic blocks to create physical crosslinks that give the material its mechanical properties (see page 8 column 2 paragraph 1). Specifically, Bezemer et al. teach poly(ether ester amide) multiblock copolymers composed of poly(ester amide) blocks and poly(ether ester amide) blocks (see Scheme 2). The distinction between the two blocks in the polymer is that in one an aliphatic diol is used while in the other a PEG diol is used. Variation in the proportion of aliphatic diol to PEG controls the rate of degradation of the polymer and the rate of drug release (see page 9 column 1 paragraph 1, figures 7 and 8)

Polymers composed of CADA monomers were known at the time of the invention. In addition, the selection of a linear C_8 α, ω dicarboxylic acid for C, leucine for A, and a hexyl diol or PEG for D were specifically taught. In the case of the hexyl diol the CADA polymer is a poly(ester amide) while the case of PEG diol could be referred to as a poly(ether ester amide). In light of both Katsarava et al. and Katsarava et al. reference B, these two polymers that compose the two blocks of the elected polymer would have been obvious to one of ordinary skill in the art at the time of the invention. The elected polymer, like that of Bezemer et al., is a multiblock copolymer composed of poly(ester amide) blocks and poly(ether ester amide) blocks that differ only in the use of an aliphatic diol or PEG diol in its construction. The exchange of the aliphatic diol for a PEG diol in blocks of the polymer allows modulation of the release of drug such that the drug release rate and degradation rate increases as the poly(ethylene glycol) proportion increases (see figures 7 and 8). Further, based upon the teachings of Nagata the integration of this PEG segment into the poly(ester amide) would be expected to confer

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additional avenues of enzymatic degradation *in vivo* where the resulting poly(ether ester amide) would be more susceptible to enzymatic degradation. This would have been desirable to one of ordinary skill in the art at the time of the invention to afford them greater control over the rate of drug release from a coating on a medical device. By parallel, it would have been obvious to one of ordinary skill in the art at the time of the invention to construct a polymer like that of Bezemer et al. based on the poly(ether amide)s of Katsarava et al. in view of Katsarava et al. reference B (applying a known technique to improve a similar product). This modification would be expected to provide the ordinarily skilled artisan greater control over the rate of drug release from the polymers of Katsarava et al. in view of Katsarava et al. reference B as well as mechanical integrity as taught by Bezemer et al. Taking the 8-L-Leu-6 polymer taught by Katsarava et al. reference B as the base poly(ester amide), the result of this modification is the elected polymer. It then follows that the application of this polymer to a device surface as taught by Katsarava et al. would also have been obvious.

Since condensation of a diol with an amino acid was a known synthetic route for producing the diol-diamines in the CADA units and PEG was a known diol, it would have been obvious to one of ordinary skill in the art at the time of the invention to use this same route to produce the PEG-diester-diamine (a PEG version of a diol-diamine where a PEG-diester is the “diol”) for the PEG containing CADA monomer unit (see Katsarava et al. reference B scheme 1; instant claims 21 and 34). To produce the elected polymer made by obvious by the combination of both Katsarava et al. references Nagata, and Bezemer et al. there would need to be a molar amount of the

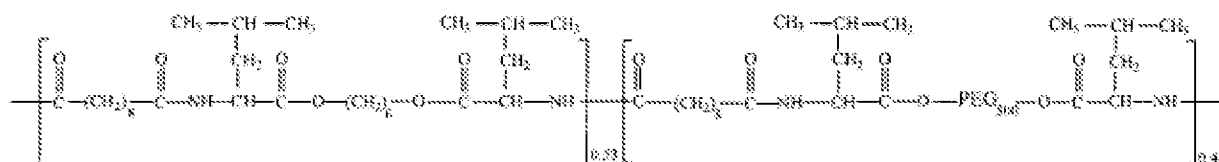
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dicarboxylic acid equal to the total molar amount of the diol-diamine and the PEG-diester-diamine such that each monomer unit would have one dicarboxylic acid moiety. So if X is the molar amount of diol-diamine and Y is the molar amount of PEG-diester-diamine, there would need to be $X + Y$ moles of dicarboxylic acid (see instant claim 23). Based upon the teachings of Bezemer et al. that the proportion of PEG containing blocks in the poly(ether ester amide) controls the rate of degradation and drug release from the polymer as well as the teachings of Nagata that the longer PEG chains in the polyester result in a faster rate of enzymatic degradation (see figure 4), it would have been well within the purview of one of ordinary skill in the art to optimize such monomer/reactant proportions and PEG chain length as a matter of routine experimentation. Thus it would have been obvious to one of ordinary skill in the art to employ the elected polymer as a coating on an implantable substrate of a medical article as well as fabricate the article via the claimed method. Therefore claims 1, 3-6, 13-15, 19-21, 23-27, 34-36, and 40-41 are obvious over Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al.

Claims 1-2 and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al. as applied to claims 1, 3-6, 13-15, 19-21, 23-27, 34-36, and 40-41 above, and further in view of Michal (previously cited).

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Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al. make obvious a coated medical article and its claimed method of production where the polymer coating includes the elected poly(ester amide)



Although this modified reference does teach the medical article to be one that contacts blood, it does not explicitly teach the article is a stent. Michal teaches stents with a series of polymeric coatings (see Katsarava et al. paragraph 47). In particular, Michal teaches biodegradable polymers being used as an overcoat on stents and specifically name poly(ester amide)s as envisioned polymers for such a purpose (see paragraphs 15 and 26; instant claims 2 and 22). In view of the teachings of Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al. that the poly(ester amide)s can be used in implanted devices that contact blood, it would have been obvious to one of ordinary skill in the art at the time of the invention to select a stent as one such device. Therefore claims 1-2 and 21-22 are obvious Katsarava et al. in view of Katsarava et al. reference B, Nagata, Bezemer et al., and Michal.

Response to Arguments

Applicant's arguments, filed June 30, 2009, have been fully considered but they are not deemed to be persuasive. Nevertheless an additional reference is cited to add

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support to the previous rejection over Katsarava et al. in view of Katsarava et al. reference B and Nagata.

Regarding rejections under 35 USC 103(a) over Katsarava et al. in view of Katsarava et al. reference B and Nagata:

In contrast to Applicant's characterizations of the previous rejection, the determination of obviousness of the instant invention is neither blithe nor requires Applicant's compounds as templates. The combination of Katsarava et al. in view of Katsarava et al. reference B, Nagata and Bezemer et al. provides a template for the instantly claimed polymers well as demonstrates motivation for one of ordinary skill in the art to have made them and the claimed coated medical device at the time of the invention. Applicant's emphasis on the supposed lack of motivation to replace "one and only one of the hexanediol elements in the CADA-CADA" polymer with PEG diol is not persuasive since 1) the CADA polymer has only one diol that could be replaced and 2) Katsarava et al. teach the diols used to make their disclosed polymers include hexandiol as well as poly(ethylene glycol). Applicant further argues that the types of polymers taught in Nagata are entirely different than those of the Katsarava et al. references. While the Nagata polymers do not contain amide moieties like those of the Katsarava et al. references, all three references teach polymers with aliphatic polyester segments. For this reason, the effect of incorporating polyether chains into such polymers is pertinent to the polymers of Katsarava et al. and Katsarava et al. reference B.

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Regarding rejections under 35 USC 103(a) over Katsarava et al. in view of Katsarava et al. reference B, Nagata and Michal:

Applicant's arguments reiterate those made against the rejection over Katsarava et al. in view of Katsarava et al. reference B and Nagata. Those arguments were address above and are similarly reiterated here.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615